<u>Temperamental vulnerability to emotion dysregulation and risk for mental and physical health challenges</u>

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Abstract:

Emotion dysregulation characterizes many forms of psychopathology. Patterns of dysregulation occur as a function of a developmental process in which normative and adaptive emotion regulation skills fail to become part of the child's behavioral repertoire due to biological, psychological, and contextual processes and experiences. Here we highlight the processes involved in the dysregulation of temperamental anger and frustration that become core features of externalizing problems and place children at risk for more serious forms of psychopathology. We imbed these processes in a larger self-regulatory framework, and we discuss how they influence mental as well as physical health, using data from our 20-year longitudinal study following a large cohort of children into young adulthood. Recommendations are made for future research involving the integration of biological systems with mental and physical health outcomes.

Keywords: emotion dysregulation | development | temperament | biopsychosocial model | mental health | physical health

Article:

A quarter century of research and theorizing about the role of emotion regulation (ER) in adaptive and maladaptive functioning was stimulated in part by foundational work in the discipline of developmental psychopathology (cf. Cicchetti, Ackerman, & Izard, 1995). This perspective, with its emphasis on understanding and characterizing mechanisms of development and describing developmental processes across multiple levels of analyses (Cicchetti, 1984, 1993; Cicchetti & Rogosch, 1996; Sroufe & Rutter, 1984), is well suited to study the role of ER in development. ER is, by its very nature, a dynamic process involving biological, psychological, and social processes interacting across time. In addition, it is a central mechanism in pathways to adaptive and maladaptive outcomes, pathways that may be characterized by multifinality and equifinality (Cicchetti & Rogosch, 1996). More specifically, and as highlighted in this Special Issue, the notion of *emotion dysregulation* is considered a critical factor in the emergence of problematic behavior during development, with the premise that dysregulation of emotion underlies many forms of psychopathology (Beauchaine, 2015).

In addressing the factors that contribute to dysregulated patterns of ER, we must acknowledge that there are normative developments in ER and that, regardless of what inferences we can reliably make and what challenges the measurement of such processes pose, children typically acquire a set of emotion skills that enable them to cope with a wide range of social and nonsocial challenges (see Calkins & Perry, 2016; Kopp, 1982, for reviews). Understanding these normative processes, and the potential sources of individual differences in them that may initiate a pathway to risk for later psychopathology, is fundamental to understanding how emotion dysregulation emerges and contributes to maladaptive outcomes.

Our definition of ER is consistent with many of our colleagues (Cole, Martin, & Dennis, 2004; Eisenberg, Hofer, & Vaughn, 2007; Gross & Thompson, 2007; Thompson, 1994) and highlights the central role that emotional processes play in child functioning, as well as the measurement of these behavioral and biological processes in emotionally salient situations (Calkins & Hill, 2007). We define ER as a set of processes that function at biological, behavioral, and social levels. Specifically, these processes capture complex biological responses and dynamic behaviors that are both automatic and unconscious, as well as conscious and effortful. ER processes serve to modulate, maintain, inhibit, or enhance the intensity and valence of emotional experiences to accomplish (and sometimes undermine) an individual's goals (Calkins & Hill, 2007). Further, these processes are not only intrinsic to the individual but also cannot be separated from their social context; emotions can be regulated even as they are regulating an individual's interactions with the environment (Cole et al., 2004). Because we take a biopsychosocial perspective on the normative development of ER (Calkins, 2011), we view an understanding of emotion dysregulation and its role in psychopathology as fundamentally a consequence of disruptions to the development of normative biological, psychological, and social processes.

In our work, we have studied the role of ER processes in the emergence and maintenance of early childhood externalizing problems (e.g., Calkins, Graziano, & Keane, 2007; Hill, Degnan, Calkins, & Keane, 2006; Perry, Calkins, Dollar, Keane, & Shanahan, 2017). Our starting point for this work was a conceptualization of early externalizing problems whose origins are in the dysregulation of temperamental frustration or anger (Calkins, 1994). Our original model linking temperament to externalizing problems hypothesized that (a) the key normative developments in ER are constrained by biological processes that may have a genetic basis, and (b) the response of parents and peers to maladaptive ER behaviors plays a role in the display of more serious behavior problems such as aggression, oppositional behavior, and conduct disorder.

Although many of these early ideas about the role of temperament, ER, and behavior problems have been confirmed by our work and the work of others (e.g., Calkins & Dedmon, 2000; Degnan, Calkins, Keane, & Hill-Soderlund, 2008; Eisenberg et al., 1996; Eisenberg et al., 2001; Gilliom & Shaw, 2004; Morris, Silk, Steinberg, Terranova, & Kithakye, 2010; Stifter, Spinrad, & Braungart-Rieker, 1999), our research also suggests a much richer conceptualization of developmental processes linked to ER and externalizing, and one that prescribes an empirical approach that is both more integrative and more nuanced than our early work. First, our work

confirms that ER itself becomes highly integrated into other biological, psychological, and social developmental processes over the course of childhood and adolescence. As such, we have adopted an empirical approach that captures child and adolescent functioning at a broader level, incorporating multiple indicators of psychological and physical health and health risk behaviors. Specifically, we note that ER itself is part of a larger system of control, or *self-regulation*, that emerges in development, and that this system includes biological, emotional, and cognitive mechanisms that become integrated over the course of development (Calkins & Fox, 2002).

Second, we note that there are multiple aspects of the child's context that will affect the child in different ways at different points in development. In addition, although we acknowledge the power of a temperament perspective, with its emphasis on biological and genetic constraints, on the development of both dysregulated patterns of ER and risk for psychopathology, we also explore factors external to the child, notably parenting and parent functioning, and peers and school experiences, as key contextual moderators. Third, we are mindful of the larger developmental process itself, one that comes with different tasks at different ages, and that provides windows of opportunity versus challenge to children's functioning.

In addition, we, along with others, are finding support for the notion that ER may directly or indirectly influence physical health, and that the biological mechanisms that underlie ER are also affecting health-related processes in both the short and the long term. This integrated view of functioning implies that the study of dysregulated ER and its role in psychopathology may be more usefully approached by considering the larger context for children's mental and physical well-being. Approaching the study of dysregulated ER in this integrated way would allow for an acknowledgment that adaptive functioning at both the psychological and the physical level may be impacted by some of the same factors that come into play in the development of ER processes, as well as highlighting the way in which psychological and physical well-being may influence one another.

As an overview, then, in this paper, we briefly review some fundamental tenets underlying our work on ER and early externalizing behaviors by focusing on normative development and sources of individual differences in ER, with an emphasis on temperament and parenting. We provide an overview of the larger self-regulatory system, with a specific emphasis on biological control mechanisms that support the development of normative skills of ER and, when compromised, potentially underlie dysregulation. We highlight findings from our own longitudinal work focusing on temperamental negative emotionality, notably anger, and its role in both ER and externalizing problems. Finally, we address directions for future work by discussing new data highlighting the role that ER and other self-regulatory skills play in physical health development and discuss possible mechanisms for linking mental and physical health risk outcomes.

ER: Normative Development and Individual Differences

In early influential work, Kopp (1982, 1989) provided a comprehensive overview of the development of ER in infancy and toddlerhood. ER across the first few months of life is controlled largely by innate and automatic physiological mechanisms (Kopp, 1982) and is almost entirely embedded within the infant–caregiver dyad (Sroufe, 1996). Over the course of

development, there is a gradual transition from primary reliance on coregulatory processes between infants and their caregivers, to increasing levels of independent self-regulation (Sameroff, 2010). Over time and through repeated interactions across early childhood, ER skills, strategies, and abilities that were once facilitated by caregiver support are thought to become integrated into the child's own self-regulatory skill set.

The increased ability to independently manage emotional states that emerges over the second and third year of life is highly dependent on cognitive control mechanisms including attentional, effortful, and other executive control processes (Kopp, 1989). The regulation of attention, however, is thought to be most central to the development of ER (Rothbart & Sheese, 2007) because orienting attention toward a stimulus, or away from it, has the effect of amplifying or reducing the emotional valence with which it is associated, therefore changing the emotional experience and potential salience for the child (Rothbart, Posner, & Rosicky, 1994; Rothbart, Sheese, Rueda, & Posner, 2011). As attentional neural networks mature, and increased inhibitory control emerges, children begin to effortfully redirect attention using more complex distraction strategies such as shifting attention to less emotionally relevant aspects of a situation or engaging in an entirely new activity (Grolnick, McMenamy, & Kurowski, 2006). As inhibitory and attentional processes become increasingly integrated, children become more able to delay gratification and comply with adult demands, skills that are central to the transition to formal schooling and more independent social relationships.

ER develops less rapidly and becomes more stable from early childhood on (e.g., Raffaelli, Crocket, & Shen, 2005). Both biological and behavioral aspects of ER, however, continue to be refined into middle childhood and adolescence. As children mature and become better able to identify long-term consequences of their behavior, they are better able to distinguish the effectiveness of long- and short-term regulatory strategies (Moilanen, 2007). Middle childhood and adolescence are also times during which children increasingly identify more goals, specifically social goals, for regulating their behaviors. Older children, for example, expect that displays of negative emotion are damaging to peer relationships, particularly when the goal is to take care of another's feelings; children therefore engage in more sophisticated regulation strategies to "mask" these negative emotions in front of peers (Shipman, Zeman, & Stegall, 2001; Zeman & Shipman, 1998).

Although there are clear milestones for the development of ER skills that emerge over the course of childhood, there are also individual differences, with some children developing such skills earlier than others or employing the skills they have developed more readily in emotionally challenging situations. Our conceptualization of ER argues that there are constraints on the emergence of ER and its deployment, and these constraints are at least one source of individual variation in ER and the dysregulation of emotion. We view these constraints as temperamental in origin, with temperament defined as relatively stable early differences in emotional, attentional, and behavioral reactivity that have a genetic and biological basis (DiLalla & Jones, 2000; Goldsmith, Lemery, Aksan, & Buss, 2000; Shiner et al., 2012). Specifically, infants will differ initially in their threshold to respond to visual or auditory stimuli, as well as in their level of reactivity to stimuli that may elicit negative affect (e.g., Calkins, Fox, & Marshall, 1996). This threshold is biologically based and thus, early in development, may place limits on the extent to which the child is able to exert self-regulation over arousal or be responsive to the efforts of

others to intervene (Calkins, 2011). In this way, dysregulated responding, particularly in emotionally challenging situations, may have *cascading effects* on the development of ER skills early in development, and on the achievement of subsequent emotional, social, and academic skills later in development (Masten & Cicchetti, 2010).

Another source of individual differences in ER is the context in which children are trying to learn to regulate. Variability in parental response to infants is one such contextual source of individual differences. ER theorists have long argued, for example, that secure attachment relationships, developed through sensitive and supportive caregiver behavior, lead to expectations that caregiver intervention will be both available and effective at reducing arousal (Sroufe, 1996). Moreover, a secure relationship increases children's expectations regarding their own ability to respond to environmental challenges. As a result of more independent exploration and confidence in one's own abilities to engage in and navigate through emotionally charged situations, a shift from dyadic to self-regulation occurs, resulting in increased self-regulatory capabilities (Sroufe, 1996; Thompson, 1994). Thus, parents play a key role in the normative acquisition of ER skills.

However, variations in how parents respond, or what response is elicited by variations in infants' temperamental emotionality, may undermine both the relationship and the development of ER skills. For example, some infants are more prone to cry or fuss; how caregivers respond to those displays of negative emotionality will affect the infant's ER both in the moment and over time. A large body of work assessing caregiving influences on the development of ER during early childhood has also focused on parental emotion socialization practices. Parental support of negative emotions, through problem solving, emotion-focused responses such as comforting, and expressive encouragement, is thought to enable children to accept and manage their negative emotions in effective ways (Eisenberg & Fabes, 1994; Gottman, Katz, & Hooven, 1997). Conversely, punitive and minimizing responses are believed to be particularly problematic for the development of ER because these parental reactions communicate nonacceptance of negative emotional expression and a focus on suppressing negative affect (Gottman, Katz, & Hooven, 1996; Jones, Eisenberg, Fabes, & MacKinnon, 2002). By punishing or minimizing negative emotions, parents may miss the opportunity to teach children effective coping strategies, they may increase children's personal distress, or they may come across as judgmental and undermine children's sense of self (Eisenberg et al., 1998). Thus, parents are one key element of a complex developmental process that underlies the development of ER skills.

Biological Self-Regulation Processes Supporting the Development of ER

Implicit, and sometimes explicit, in the large body of work on ER is the acknowledgment that ER is never a purely emotional process (Barret, Fox, Morgan, Fidler, & Daunhauer, 2012; Thompson, Lewis, & Calkins, 2008). ER draws on fundamental neural, physiological, cognitive, and behavioral processes, all of which become elaborated and integrated over the course of development. Moreover, ER, and other behavioral and cognitive control processes, are linked in fundamental ways to more basic biological and attentional processes, and have consequences for later-developing and more sophisticated social and cognitive skills. In addition, we, like some of our colleagues (Barret et al., 2012; Blair & Razza, 2007; Eisenberg et al., 2007; Rothbart & Sheese, 2007), embed these processes within the larger construct of *self-regulation*. Thus, the

development of ER extends from the emergence of basic and automatic regulation of biological processes in infancy to the more self-conscious and intentional regulation of behavior and cognition in middle childhood and adolescence (Ochsner & Gross, 2004). Fundamental to this developmental process is the maturation of different neural systems and processes that provide a functional mechanism for the behavioral integration we ultimately observe as children mature (Dennis, O'Toole, & DeCicco, 2013; Lewis, Todd, & Xu, 2010). Thus, the development of ER skills is marked by continuous change across biological systems that support, among other processes, the behavioral control of emotion.

There are multiple biological systems involved in ER development, but all are fundamentally supported by neural development. For example, attention skills are supported by an early emerging neural system, the executive attention network, composed of the anterior cingulate cortex in the medial frontal lobe and parts of the prefrontal cortex (Posner & Fan, 2008). These brain regions are thought to serve to coordinate, regulate, and process information from other neural networks and are involved in the control of both cognition and emotion (Posner, 2012; Posner, Rothbart, Sheese, & Tang, 2007). Greater efficiency in synaptic connections and more integrated interregional pathways within these brain regions may increase the speed at which children process the environment and allow children to better attend to specific aspects of the context or situation. This attentional control may then support children's cognitive flexibility and ability to inhibit dominant behavioral responses in favor of an alternative solution when necessary, both of which may be particularly helpful when children are required to regulate their emotions. Greater connectivity within the executive attention network, and accompanying changes in cognitive and attentional control skills, may facilitate greater use of flexible and effective strategies for the modulation of emotional arousal.

Although underlying neural connectivity and functioning are critically important to ER, much of the empirical work that focuses on underlying physiological components highlights the maturation of the autonomic nervous system (ANS) as playing a fundamental role in the regulation of emotion (Santucci et al., 2008). Although often considered separate biological systems, neural and physiological processes operate as feedback systems. The ANS, for example, is composed of a complex system of afferent and efferent feedback loops that are integrated with other neurophysiological and neuroanatomical processes, reciprocally linking cardiac activity with central nervous system functioning (Calkins & Marcovitch, 2010; Chambers & Allen, 2007); both the parasympathetic and the sympathetic branches of the ANS play a role in this heart–brain connection.

Parasympathetic nervous system (PNS) functioning in particular is theorized to be at least partially responsible for differences in the development of emotional expression and regulation. The functional status of the PNS is reflected through vagal control of the heart (Porges, 2007). Specifically, the myelinated vagus nerve (i.e., 10th cranial nerve) provides input into the heart, producing dynamic changes in cardiac activity that allow the body to transition between sustaining metabolic processes and responding to environmental stimuli (Porges, 2007). Of particular interest to researchers studying ER has been measurement of vagal regulation of the heart when individuals are emotionally challenged. During situations that do not elicit emotional arousal, the vagus nerve inhibits the sympathetic nervous system's influence on cardiac activity through increased parasympathetic influence, thus producing a relaxed and restorative state (Porges, 1995). When the environment places an external or emotionally taxing demand on the child, vagal influence is withdrawn or suppressed, resulting in increased sympathetic activity. The increase in sympathetic influence leads to an increase in heart rate, which facilitates the focused attention essential for generating emotional responses that are effective in modulating arousal (Bornstein & Suess, 2000). In this way, the withdrawal of PNS influence during emotional challenge, as evidenced by decreased vagal activity, can be used as an indicator of an individual's physiological regulation of emotion. Decreases in respiratory sinus arrhythmia (RSA) from a baseline state to engagement during emotional challenge (indicative of decreased vagal activity and a withdrawal of parasympathetic influence) are thought to better reflect physiological regulation of arousal.

Empirical work supports the association between decreases in RSA to challenge and ER in the moment and over time (Beauchaine, 2001, 2015; Buss, Goldsmith, & Davidson, 2005; Perry, Calkins, & Bell, 2016), as well as fewer externalizing (Calkins, Blandon, Williford, & Keane, 2007; Calkins & Keane, 2004; El-Sheikh, Harger, & Whitson, 2001; Graziano, Keane, & Calkins, 2007) and internalizing (Calkins, Blandon et al., 2007; Gentzler, Santucci, Kovacs, & Fox, 2009) behaviors. Calkins and Dedmon (2000), for example, found that 2-year-olds at high risk for externalizing behavior problems showed a smaller decrease in RSA in response to emotional challenge. Moreover, these children also displayed significantly more concurrent dysregulated behavior during these tasks (characterized by negative affect and venting) than did low-risk children. In a sample of 6- to 13-year-olds, children who demonstrated greater decreases in RSA in response to a sad film clip showed more adaptive ER responses (i.e., thinking about feeling better, talking to family, or listening to happy music) and lower levels of clinician-rated depressive symptoms at a follow-up assessment (Gentzler et al., 2009).

This biologically adaptive process of RSA withdrawal likely has a genetic basis but is also thought to be supported by early infant–caregiver interactions. Porges and Furman (2011) argue that social interaction with a caregiver can calm and soothe an infant's physiological state and that caregiving may facilitate greater myelination of vagal fibers and development of the vagal system. An increase in the myelination of vagal fibers may improve the modulation of physiological arousal and enable infants to engage in greater behavioral and attentional regulation, as well as more positive social interactions.

From birth, caregivers play an essential role in regulating infants' ongoing biobehavioral states and the transition between states (Calkins, 2011). For example, responsive and sensitive caregiver behavior may influence young children's ability to regulate physiological arousal by facilitating physiological homeostasis as caregivers help children find a balance between meeting their individual needs and coping with environmental stimuli during emotionally challenging contexts (Hofer, 1987; Spangler & Grossmann, 1993). Evidence from animal models also suggests that caregiving affects infants' biological systems of regulation through the environment the caregiver provides rather than through shared inherited traits. For example, Meaney and colleagues have shown that high levels of maternal licking/grooming and arched backed nursing in rats affects the neurological systems associated with the stress response, a process that has a long-term influence on stress-related illness, certain cognitive functions, and physiological functions (Caldji et al., 1998; Champagne & Meaney, 2001; Francis, Caldji, Champagne, Plotsky, & Meany, 1999). Furthermore, cross-fostering studies demonstrate that these maternal behaviors are transmitted behaviorally through the nursing mother and not through the biological mother, indicating that early caregiving is a crucial factor in early neural development and may affect the organism's level of emotional reactivity even when he or she reaches adulthood (Calatayud, Coubard, & Belzung, 2004; Champagne & Meaney, 2001).

Longitudinal studies with human infants have been informative about the relations over time between caregiving and physiological regulation in infants. One study (Propper et al., 2008), identified children who might be at genetic risk for problems with regulation because they carried the risk allele of the dopamine transmitter gene *DRD2*. Infants without the risk allele displayed appropriate cardiac vagal regulation in a laboratory paradigm that was challenging to the infants, and this pattern held across the first year. Infants with the risk allele, however, displayed a different pattern of results, depending on the level of caregiver sensitivity to which they were exposed. For infants with the risk allele and mothers who were not sensitive, poor physiological regulation was observed across the first year. Infants with the risk allele and mothers who were sensitive displayed poor physiological regulation during assessments at 3 and 6 months of age, but by the end of the first year, their pattern of physiological responding to challenge was no different than the infants without the risk allele. This Gene × Environment interaction demonstrates that infants and caregivers each contribute to the developmental process of acquiring regulatory skills very early in development.

In sum, we view the acquisition of ER processes as a normative developmental task that emerges in the context of other regulatory processes. We note that there are individual differences in this developmental process that are the source of regulated versus dysregulated responding under conditions of emotional challenge and that such differences arise from biological, temperamental, and environmental sources. We would argue that to the extent that caregivers can provide the support for physiological control early in development, particularly through the use of physical comforting and support, children should be more successful at using attentional, cognitive, and behavioral strategies to control emotion, regardless of which temperamental tendencies they exhibit. In turn, successful physiological, attentional, and behavioral strategies prepare children to engage in interactions with caregivers, facilitating the transactional relationship that reinforces sensitive and responsive caregiving over time. However, and in the case of dysregulated emotional responding, early challenges can place the child at risk for adjustment difficulties. We address this possibility with the example from our work on the emergence and maintenance of externalizing behavior in childhood and adolescence.

Temperament, ER, and Externalizing Problems in Early Childhood

Much of the early work on ER and psychopathology focused on externalizing spectrum problems, likely because they are more easily observed and may cause greater disruptions in the family, peer, and school contexts. Disruptive behaviors such as aggression, defiance, and temper tantrums are some of the most common externalizing-type behavior problems seen in young children (Beauchaine, Strassberg, Kees, & Drabick, 2002). From a normative development perspective, as children acquire more cognitive, linguistic, and regulatory skills, they are better able to cope with emotional and social challenges and thus "outgrow" these types of problem behaviors (Campbell, 2002; Kopp, 1982). Much research has shown a normative developmental

pathway of externalizing-spectrum behavior problems that peaks during the second year and shows a distinct decline with age (Hartup, 1974; Tremblay, 2000).

The emphasis on ER as a predictor of behavior problems is logical because excessive emotional lability and reactivity, and a lack of behavioral and emotional regulation, are considered core symptoms for children with externalizing-type behaviors (Gilliom & Shaw, 2004; Keenan & Shaw, 2003). Children who show high stable expressions of anger across development, in particular, are at greater risk for difficulties across a range of social and nonsocial domains (e.g., Cole, Teti, & Zahn-Waxler, 2003; Eisenberg et al., 2001). Children who are quicker to experience intense anger without the ability to modulate that arousal are more likely to engage in maladaptive behaviors (Vitaro, Brendgen, & Tremblay, 2002), which undermine functioning in a variety of ways and lead to externalizing behaviors, negative peer interactions, poor social problem-solving abilities, and academic difficulties (Casey & Schlosser, 1994; Cole et al., 2003; Eisenberg, Fabes, Nyman, Bernzweig, & Pineulas, 1994).

Much of the work on anger, and subsequent dysregulated ER and externalizing, has focused on understanding its origins, particularly its genetic and biological origins. Studies involving twins and adoptees provide evidence of an underlying genetic contribution to individual differences in infants' and children's expression of anger (e.g., Deater-Deckard, Petrill, & Thompson, 2007; Gagne & Goldsmith, 2011; Goldsmith, Buss, & Lemery, 1997; Saudino, 2005), accounting for perhaps 40%–70% of the variance in the trait. Evidence for the genetic contribution to trait-level anger also comes from molecular genetic studies. Specifically, the underlying biology of anger and aggression has implicated the dysregulation of serotonergic activity (e.g., Virkkeuen & Linnoila, 1993), although this association may function differently for males and females (Suarez & Krishnan, 2006). The dopamine D4 receptor (*DRD4*) gene, the norepinephrine system receptor gene *ADRA2A* (Comings et al., 2000), and the *TBX 19* gene (Wasserman, Geijer, Sokolowski, Rozanov, & Wasserman, 2007) have each also been implicated as a candidate gene for anger, along with additional temperamental traits (Saudino, 2005).

Although temperamental anger is moderately to substantially heritable, identification of which genes under which conditions produce anger and dysregulation of anger has been more challenging (e.g., Pickles et al., 2013). From a translational perspective, however, it may be of more value to identify the conditions under which a propensity toward intense and/or frequent experiences and expressions of anger evolves into dysregulation of anger under conditions of challenge and how that pattern of regulation becomes increasingly disruptive to adaptive functioning across time and contexts. This has been the goal of our research program for the last 25 years. Much of this work has involved a three-cohort longitudinal study, the RIGHT Track Project, of nearly 450 children and their families followed from child age 2 to young adulthood, (Blair et al., 2016; Blandon, Calkins, Keane, & O'Brien, 2008; Calkins, Graziano, & Keane 2007; Calkins & Keane, 2004; Dollar, Perry, Calkins, Keane, & Shanahan, 2018; Perry et al., 2017; Smith et al., 2004). Mothers of several hundred children from the community completed a behavior problems questionnaire, with a particular focus on externalizing problems (Achenbach, 1991, 1992), which assessed a broad array of toddler behaviors. We oversampled for children who were behaviorally at risk, with 30% of these toddlers identified by their mothers as being particularly difficult to manage (had more temper tantrums, were more difficult to soothe, became more easily frustrated, and cried more frequently, compared to the typical 2year-old; see Calkins, Dedmon, Gill, Lomax, & Johnson, 2002, for a full description of recruitment procedures and participant characteristics). At ages 2, 4, 5, 7, 10, 15, and 17, participants were assessed across multiple domains of functioning (biological, emotional, behavioral, and cognitive self-regulation; relationships with caregivers, peers, and teachers; psychological, social, and academic adjustment). At ages 15, 16, 17, and 19 years old, participants completed laboratory health visits, including reporting on their health-related behaviors (e.g., nutrition, substance use, exercise, and sleep) and mental health. In addition, trained research assistants conducted blood draws, and obtained measures of weight, height, and adiposity.

Our methodology was explicitly multi-informant, and we gathered data from mothers and fathers, teachers, and the children themselves, observationally and self-reported, and by the collection of cardiac and neural measures. As an anchor for all of our findings, we should note that approximately 10% of our sample, and roughly equal numbers by sex, met clinical criteria for externalizing spectrum problems via the Child Behavior Checklist, with 13%–24% meeting diagnostic criteria for attention-deficit/hyperactivity disorder, oppositional defiant disorder, or conduct disorder across the age period 10–17 years using clinical interviews. Thus, although we frame our work in explicitly normative developmental terms, our sample is sufficiently diverse in terms of functioning to address questions about risk for psychopathology.

For illustrative purposes, we review a selection of findings from this work that support the idea that normative temperament and emotion processes that emerge in early development may be altered such that, over time, children engage in patterns of emotion dysregulation that undermine functioning in multiple domains. Initially, our goal was to test a model of the role of frustrated temperament and ER, moderated by sensitive caregiving, as a predictor of multiple outcomes, including externalizing behavior (Calkins, 1994). In our longitudinal work focused on the preschool period, we confirmed that maternal behavior, namely, sensitivity and the mother-child attachment relationship, predicted emotionality and ER (Smith, Calkins, & Keane, 2006), and that maternal behavior and frustration reactivity predicted increases in externalizing behavior across the preschool period (Calkins, Blandon, et al., 2007). We were also interested in the extent to which physiological process, namely, vagal regulation under conditions of challenge, would differentiate children with early behavior problems from those without such problems. We confirmed that lower vagal regulation was a characteristic of children with early externalizing problems (Calkins, Graziano, et al., 2007), and that poorer vagal regulation and a low-quality mother-child relationship accounted for worsening of behavior problems from age 2 to age 5 (Calkins, Graziano, Berdan, Keane, & Degnan, 2008). Moreover, these temperamental (Berdan, Calkins, & Keane, 2008), emotional (Keane & Calkins, 2004), and biological (Graziano et al., 2007) processes were also clear predictors of other indicators of potentially problematic outcomes, including lower peer status and social preference as early as kindergarten.

Although our early work focused on the *predictors* of ER and externalizing behavior problems, the nature of our longitudinal study has allowed us to examine patterns of *growth and change* in both ER and externalizing problems. For example, we found that children with high and stable trajectories of externalizing problems across toddlerhood and preschool were characterized by poor physiological regulation and low maternal control during toddlerhood (Degnan et al., 2008). In addition, although on average children display a pattern of increased ER skills over the

preschool period, we have observed that early child and environmental factors affect this growth; specifically, we found that maternal depression was predictive of less steep increases in ER trajectories while greater physiological regulation was predictive of steeper increases (Blandon et al., 2008).

Our approach to understanding the early emergence of ER, externalizing problems, and social functioning has also emphasized understanding the processes and mechanisms involved, as opposed to simply identifying predictors of these behaviors. A process-focused analytical approach has involved testing different types of models, including transactional, mediational, and cascade models, to understand how different factors might work across time and across domains. Therefore, central to the transactional model is the analytic emphasis placed on the bidirectional, interdependent effects of the child and environment (Sameroff, 2009). We utilized this approach with our data to examine the transactional association between RSA withdrawal during a frustration task and maternal sensitivity from age 2 to age 5 (Perry, Mackler, Calkins, & Keane, 2014). Our goal was to assess whether parenting facilitated changes in children's physiological regulation of emotion, and whether children's physiological regulation influenced the parenting that children subsequently received. We found that maternal sensitivity at age 2 was associated positively with RSA withdrawal at age 4, and RSA withdrawal at 4 years was associated positively with maternal sensitivity at 5 years. These results suggest that after controlling for the stability in sensitivity over early childhood, early sensitive maternal responding may facilitate the development of physiological regulation, which in turn may make children easier to parent, thereby eliciting greater maternal sensitivity at later time points.

As the children in our study transitioned through middle childhood into preadolescence, we began using developmental cascade models to investigate the processes that might link ER to psychological and social outcomes during this time of transition that is marked by maturing biological mechanisms, the emergence of sophisticated behavioral skills, and the entrance into more complex social environments. Such models are based on the expectation that development in one domain will shape development in other domains in a progressive cascade (Masten, Burt, & Coatsworth, 2006). In our work, we found ER processes in early childhood predicted specific patterns of positive and negative social behavior (cooperation, leadership, and direct and indirect aggression) and social skills in middle childhood, which in turn predicted friendship quality (Blair et al., 2015) and peer acceptance and rejection (Blair et al., 2016) in preadolescence. The developmental skills that come online during middle childhood and adolescence are thus constrained to a degree by early ER processes and may exacerbate existing risk for compromised social development as children transition to adolescence.

By the time children reach adolescence, the skills needed to regulate emotions in the home, school, and peer group contexts are sophisticated and likely incorporate the full complement of regulatory abilities to manage physiology, attention, emotion, and cognition. For this reason, when we examined longitudinal patterns of externalizing behavior across childhood and adolescence, we considered several different self-regulatory processes within the context of one another, thereby enabling us to identify the most potent predictors of patterns of problem behavior across time. Moreover, we adopted a person-centered approach and identified distinct patterns of behavior from the preschool to adolescence period. Consistent with existing work, the results from this study suggested the existence of four distinct patterns of externalizing behavior

from ages 2 to 15: high stable, declining, low stable, and adolescent onset. Of interest to us was the contrast of the high stable group versus the normative decline group in terms of how distinct self-regulatory processes during the critical preschool transition of ages 2–5 years differentially predicted membership in the two groups. We found that none of the indicators of self-regulation at age 2 predicted externalizing group membership. However, at age 5, both dysregulated anger and poor inhibitory control distinguished the high stable and the normative declining groups. Children who were able to control their emotions and inhibit their actions at this age were more likely to experience normative declines in externalizing behavior than those whose behavior remained problematic through childhood and adolescence (Perry et al., 2017). Thus, selfregulatory skills by the end of early childhood, a time during which self-regulatory development slows and most children transition to the academic environment, may be more strongly associated with externalizing trajectories over time than self-regulatory abilities in toddlerhood when these abilities are underdeveloped.

In sum, this work illustrates some of the fundamental tenets of our approach to the study of temperament, ER, and early externalizing behavior problems as risk factors for psychopathology. First, we note that emotional processes recruit and integrate multiple psychological functions, some of which themselves are regulatory in nature (attention, appraisal, cognitive processing, and motor responding; Lewis & Steiben, 2004). Thus, it is clear that emotions and their regulation have the capacity to organize and facilitate, or disorganize and disrupt, other psychological and social processes (Calkins & Hill, 2007; Cole et al., 2004; Gray, 2004), both in the moment and at the level of the emergence of these skills over the course of early development (Bell & Wolfe, 2004). Our work demonstrates that, to the extent that children understand and control emotions successfully, they have a greater opportunity to attend to, assimilate, and process events in the world around them, thus enhancing psychological, social, and academic competence (Blair et al., 2015; Dollar et al., 2018; Hill et al., 2006; Perry et al., 2016, 2017).

A second tenet of our approach that we have examined extensively is the principle that ER develops within a social context, with a normative transition from other regulation to self-regulation occurring over the first several years of life (Sameroff, 2010). This process is transactional, and therefore the developmental process of acquiring ER skills is dynamic; opportunities for success or failure of dyadic interaction that facilitates ER occur frequently and vary depending on the developmental demands on the child and the psychological and contextual demands on the parent. Although we acknowledge that trait-level factors are at play (for both parent and child), the pathways from early temperament to later externalizing behaviors are multifactorial and constrained to some degree by the development level of the child and its associated caregiving demands. Moreover, and particularly in very early development, these interactions will have consequences not only for the child's behavior, but for biological processes as well. To the extent that foundational processes are compromised, the likelihood of a positive developmental outcome is diminished.

Future Directions: Integrating Self-Regulation, Psychological Functioning, and Physical Health Risks

Our recommendations for future research focus on the integrated nature of development and the need for the field of developmental psychopathology to consider the myriad ways in which aspects of children's lived experience across multiple domains of functioning intersect. Here we draw on some of our own observations of these intersections as they impact children's and adolescents' adaptations at the levels of psychological and physical health.

Self-regulation and health risk

For the most part, the questions we addressed early in our work and the analytical approach we used in the latter half of the study echoed themes that are consistent with a developmental psychopathology approach. As with any longitudinal study, though, serendipitous observations have also led us in new directions. For example, embedding ER in a larger self-regulatory framework was largely the result of having observed the regulatory role that other psychological and biological processes play in children's responding to the challenge tasks we posed. A second unexpected direction we took with this work, having to do with consideration of physical health, was the result of findings about children's physical growth we observed because of the need to covary anthropometric measures (height and weight) from cardiac measures. We noted that by the age of 5 years, 35% of our sample met the criteria for obesity, or borderline obesity, as defined by the World Health Organization (2008). This led to a series of papers examining the role of self-regulatory processes in the emergence of obesity and increases in weight across childhood. Our findings across this work revealed that multiple measures of self-regulation at age 2 were predictive of obesity at age 5 (Graziano, Calkins, & Keane, 2010), including poor vagal regulation of cardiac activity (Graziano, Kelleher, Calkins, Keane, & O'Brien, 2013). A factor score that combined attention, emotion, and behavioral regulation at age 2 predicted increases in weight from ages 4 to 10, and this score distinguished obese from nonobese children; for every 1 SD decrease in self-regulation at age 2, there was a 74% increased probability that children would be obese at age 10 (Graziano, Calkins, Keane, & O'Brien, 2011).

These findings between self-regulation and weight gain and obesity are consistent with a growing literature highlighting how early temperamental and self-regulatory processes are associated with childhood obesity and later cardiovascular risk (CVR; Anzman-Frasca, Stifter, & Birch, 2012; Juonala et al., 2011; Miller et al., 2018; Miller, Rosenblum, Retzloff, & Lumeng, 2016; Moffitt et al., 2011). The assumption is that individuals with poor self-regulation skills are more likely to engage in emotional eating, to overeat, and less likely to engage in energy-expending physical activity (Crescioni et al., 2011; Daly, McMinn, & Allan, 2004; Gianini, White, & Masheb, 2013; Wills, Isasi, Mendoza, & Ainette, 2007). For example, in our own work we found evidence that adolescents who self-reported lower ER skills were more likely to engage in later emotional eating (Shriver et al., 2019).

Adolescence has emerged as an important time for potential increases in indicators of CVR, including obesity, elevated lipids, altered glucose metabolism, and hypertension (Ford & Capewell, 2007; Hatzenbuehler, McLaughlin, & Slopen, 2013; Ishii et al., 2012; Miller, Kaylor, Johannsson, Bay, & Churilla, 2014; Nguyen et al., 2011; Rosner, Cook, Daniels, & Falkner, 2013). Given that CVR initiates and contributes to chronic disease and predicts subsequent morbidity and mortality by young adulthood or even earlier (Hartiala et al., 2012; Janssen et al., 2005; Juonala et al., 2011), empirical work to identify early mechanisms that

influence adolescent CVR is needed to prevent or slow these early signs of CVR. We recently extended our work to examine the relations between childhood self-regulation and markers for cardiovascular disease and other health risks (sleep, exercise, substance use, and sexual behavior) in late adolescence and emerging adulthood (Wideman et al., 2016). Our main hypotheses centered around the idea that physiological, emotional, and behavioral dysregulation would negatively affect engagement in health risk behaviors, which in turn would increase the risks for CVR by altering weight, lipid profiles, glucose metabolism, blood pressure, and inflammatory markers.

In one paper addressing the role of fundamental physiological regulation processes in CVR, we found that lower cardiac vagal withdrawal measured at age 2 in response to an emotional challenge was predictive of higher diastolic blood pressure in children 14 years later during their first health assessment at age 16 (Gangel et al., 2017). Moreover, clinically significant diastolic blood pressure was predicted by RSA withdrawal at age 2. We speculate that there are several pathways from physiological regulation to CVR. Vagal regulation of cardiac function as indexed by RSA withdrawal may directly affect later CVR via its influence on the baroreflex arc (Tan & Taylor, 2010), which is involved in maintaining homeostasis in blood pressure. Decreased vagal function and lower heart rate variability have been associated with increased fasting glucose, glycosylated hemoglobin, proinflammatory cytokines, and acute-phase proteins (Thayer & Sternberg, 2006), all which have been linked to increased allostatic load and poor health (McEwen, 1998). RSA withdrawal also may indirectly influence later CVR by providing the individual with resources to engage in healthy behaviors. For example, children who have an increased capacity for vagal regulation of cardiac output may be more adept at engaging in healthy behaviors, such as strenuous exercise, which could contribute to greater plasticity in the vascular system by adolescence (Atlantis, Barnes, & Singh; 2006; Sallis, Prochasks, & Taylor, 2000). Although we cannot conclude at this point which of these hypotheses is correct, our next steps will be to examine whether physical activity, measured by both self-report and laboratory assessments, might mediate the relation between self-regulation and blood pressure.

More recently, we examined which specific self-regulatory skills (i.e., emotional, attentional, behavioral, or cognitive self-regulation) were most strongly associated with adolescent cardiometabolic risk (CMR) profiles at each time point while accounting for the interdependencies among each self-regulation skill (Wideman et al., 2019). Given that we view self-regulation as a multifaceted construct consisting of self-regulation across multiple levels of functioning (i.e., attentional, emotional, behavioral, and cognitive) that unfolds across early development, we hypothesized that in toddlerhood more rudimentary regulatory processes (ER) would predict CMR profiles, whereas later in childhood more sophisticated regulatory processes (cognitive regulation) would differentiate among CMR profiles. As expected, when examining specific probabilities of group membership, we found that children with better ER skills at ages 2 and 4, greater behavioral regulation skills in response to food and attentional regulation skills at age 4, and better attentional and cognitive regulation skills at age 7 were more likely to be in the low-risk CMR group when compared to the high-risk CMR group. Thus, results from this study indicated that the dominant self-regulation skill of each developmental period emerged as the significant predictor of patterns of adolescent CMR while accounting for the interdependencies among each self-regulation skill. Together, our early work offers preliminary support for the importance of childhood self-regulatory processes at multiple levels of analysis as early

predictors of CVR as early as adolescence. These findings suggest the importance of early intervention programs that target development of self-regulation skills to promote health-related behaviors and lower increasing rates of adolescent obesity and CMR.

Dysregulation of anger and health risk

Additional findings from our research program, in conjunction with those of other researchers, are providing support for how self-regulation is a universal skill that helps individuals to engage in healthy behaviors, as well as to resist the urge to engage in risky, unhealthy behaviors, which, in turn, may lower CVR. Emerging evidence suggests that dysregulated anger, in particular, may increase the likelihood that children will engage in risky health behaviors, such as substance use and abuse (e.g., Hussong & Chassin, 1994) and put them at risk for later CVR (e.g., Harburg, Julius, Kaciroti, Gleiberman, & Schork, 2003). This evidence builds upon a sizable literature that dysregulated anger is associated with a range of problems including behavior problems (Perry et al., 2017), social and academic maladjustment (Dougherty, 2006; Rydell, Thorell, & Bohlin, 2007), as well as physical health risk (Pardini, Lochman, & Wells, 2004). For example, anger is more strongly related to alcohol and drug use than other negative emotions (McCreary & Sadava, 2000; Pardini et al., 2004). Several hypotheses may explain why anger-prone individuals are more likely to engage in risky behaviors, including using substances to deal with intense emotions, being rejected by one's peers, and not developing important self-regulation skills to resist the impulse to engage in risk taking. For example, consistent with a selfmedication model, adolescents who reported experiencing greater anger were more likely to consume alcohol on days in which they experienced elevated negative mood (Gould, Hussong, & Hersh, 2012).

To date, longitudinal associations between anger and risky health behaviors, including substance use, are lacking, particularly studies that begin in childhood. In our work, we found that mothers who rated their children as higher on anger expression at age 5 were more likely to engage in risk-taking behaviors, including substance use and risky sexual behavior, at age 15. Moreover, results indicated that poor self-regulation, low social skills, and socializing with deviant peers in middle childhood all served as mechanisms to explain why children who express intense anger are more likely to engage in risk-taking behaviors in adolescence (Dollar et al., 2019). The results from this study provide evidence that the association between dysregulated experiences of anger and substance use begin as early as childhood, and that many experiences and skills associated with middle childhood may help to explain these associations.

There is also growing evidence of an association between anger and CVR (e.g., Gallacher, Yarnell, Sweetnam, Elwood, & Stansfeld, 1999; Kerr & Schneider, 2008; Kubzansky, Cole, Kawachi, Vokonas, & Sparrow, 2006; Williams, 2010; Williams, Nieto, Sanford, & Tyroler, 2001). For example, in a sample of adult women, experiences of heightened anger were associated with increased biological health risk, including pro-inflammatory markers (Interleukin-6 and C-reactive protein), and indices of cardiovascular malfunction (systolic blood pressure and total/HDL cholesterol ratio; Kitayama et al., 2015). Moreover, in a recent metaanalysis of 25 studies of initially healthy people and 19 studies of people with coronary heart disease, results indicated that anger and hostility were associated with coronary heart disease outcomes in both types of samples (Chida & Steptoe, 2009).

Multiple hypotheses might explain the process by which anger is associated with greater CVR (Rozanski, Blumenthal, & Kaplan, 1999). The first explanation involves individual behavioral and cognitive factors. For instance, an individual who experiences intense feelings of anger may be at a greater risk of developing CVR because the individual engages in poor health behaviors (i.e., sedentary lifestyle or substance use/abuse) and makes poor health-related decisions (i.e., high fat and high sugar diets or dysregulated eating behaviors). Another hypothesis is that the association between anger and CVR may be enhanced through cognitive processes, such as rumination, that maintain and increase discomfort, hypertension, and pain (Markovitz, Matthews, Wing, Kuller, & Meilahn, 1991; Miers, Rieffe, Terwogt, Cowan, & Linden, 2007; Schneider, Egan, Johnson, Drobny, & Julius, 1986). Individuals who experience intense anger are more likely to ruminate about their anger, thereby increasing the likelihood of hypertension, pain, and so on. Others have suggested that the association between anger and compromised physical health, such as CVR, may be explained, at least in part, by a pathway of chronic inflammation (Miller, Chen, & Cole, 2009). In support of this notion is recent work that has found evidence of positive associations between anger and inflammatory markers (Boylan & Ryff, 2013; Elovainio et al., 2011; Graham et al., 2006; Marsland, Prather, Petersen, Cohen, & Manuck, 2008). Finally, a direct physiological mechanism between anger and CVR has been proposed. Specifically, hemodynamic and neurohormonal responses of the sympathetic adrenomedullary system and of the hypothalamic-pituitary-adrenal (HPA) axis, which may be activated under conditions of anger, may explain the association between anger and CVR.

Thus, through this brief overview of the evidence highlighting that anger dysregulation is associated with both psychological and physical health, many important directions for future work become evident. For example, additional work is needed to address the longitudinal, and possibly transactional nature, of the association between anger dysregulation, and physical and psychological health. Given the sizable literature linking dysregulated anger with a range of maladaptive psychological risks (e.g., aggressive behaviors), risky health behaviors (e.g., substance use and dysregulated eating behaviors), and poor physical health (e.g., cardiovascular disease), it is imperative that future studies address the pathways by which these associations occur over time. For example, whereas it is known that psychological and physical health are often associated with one another (e.g., Copeland, Shanahan, Worthman, Angold, & Costello, 2012), the transactional nature of the association between emotion dysregulation, mental health, and various forms of physical health is largely unknown. Moreover, given that most research linking anger dysregulation with risky health behaviors and physical health outcomes has occurred in cross-sectional or short-term longitudinal studies beginning in adolescence, additional work is critically needed to address how these associations may begin earlier in life with children's temperamental tendencies and/or lack of developing appropriate anger regulatory skills.

Integration of physiological systems to study integrated psychological and physical health outcomes

Another direction for future research in ER is to develop a more integrated understanding of biological processes that are associated with ER and psychological and physical health risks. Much of the work investigating the role of biological systems and human behavior has focused

on the separate physiological correlates of emotion and ER and/or psychopathology. In addition, although it is important to understand the role of each biological system for the development of ER, it is almost certainly the case that multiple systems are working at the same time and potentially influencing a wide array of emotional and social behaviors (Buss, Jaffee, Wadworth, & Kliewer, 2018). Therefore, for example, when individuals encounter situations that require the modulation of emotional arousal, we know that multiple biological systems are activated (Calkins & Hill, 2007; Thompson et al., 2008), though the degree to which they are activated and influence subsequent behavior may vary depending on the type and intensity of stimulation and the degree to which it places demands on higher order processing versus more primitive processes. Hypotheses about how specific systems respond under which conditions can be advantageously used to address why and how particular patterns of dysregulation occur.

Increasingly, studies have explored the association between the sympathetic and parasympathetic branches of the ANS as it relates to processes integral to children's ability to regulate emotion (e.g., Beauchaine, Gatzke-Kopp, & Mead, 2007; Boyce et al., 2001; McKernan & Lucas-Thompson, 2018; Philbrook, Erath, Hinnant, & El-Sheikh, 2018). For example, Stifter et al. (1999) found that reciprocal sympathetic activation, or increases in sympathetic activity accompanied by decreases in parasympathetic activity, was associated with better ER in the preschool period. In addition, associations have been made between HPA functioning and ANS functioning in the regulation of emotion (Cole, Zahn-Waxler, Fox, Usher, & Welsh, 1996; Stansbury & Gunnar, 1994). For example, Lucas-Thompson, McKernan, and Henry (2018) found that lower baseline RSA and greater cortisol reactivity to a lab stressor was associated with fewer depressive symptoms in adolescence. However, more work is needed to better understand how HPA and cardiac systems work together in affecting children's ability to emotionally regulate given the small literature that is inconsistent in terms of its findings.

Some work has investigated how neural systems and the stress system interact during ER processes. For example, using functional magnetic resonance imaging and measures of adults' salivary cortisol, Urry et al. (2006) found that the ability to emotionally regulate, as indexed by high levels of ventromedial prefrontal cortex activation and low levels of amygdala activation, was related to the steepest diurnal cortisol slopes. These results suggest that the circuitry involved in prefrontal cortex and amygdala functioning enables effective regulation of negative emotion and is associated with the regulation of endocrine activity, which is important for mental and physical health and adjustment.

Conclusions

We view emotion dysregulation as fundamentally a consequence of disruptions to the normative acquisition of ER skills, or the inability of such skills to be activated under certain conditions. Thus, although most children acquire ER and other regulatory skills in childhood, there are clear individual differences in both the ability and the readiness of some child to enact them successfully when needed. The goal of our research has been to understand the sources of individual differences that lead children to patterns of dysregulation underlying externalizing problems in childhood and that place them at increased risk for more serious psychopathology, some forms of which increase the likelihood of school dropout, substance use, and criminality. We take an integrated view of both ER, and thus view it as part of a larger system of self-

regulation, and adaptive behavior, which we argue consists of both mental and physical wellbeing. The reciprocal relationship that clearly exists between mental and physical health, and the stability of these problems once they become established, underscores the need to enhance our understanding of the multiple pathways to emotional functioning that begin in very early development.

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